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SERVIN, Rolf [SE/SE]; Amersham Health R & D AB, P.A. Hanssons v. 41, S-205 12 Malmö (SE). **THANING, Mikkel** [SE/SE]; Amersham Health R & D AB, P.A. Hanssons v. 41, S-205 12 Malmö (SE).

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- with international search report
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/089656 A1

(54) Title: METHODS AND COMPOUND MIXTURES FOR DETERMINING PROTEIN ACTIVITY USING NMR SPECTROSCOPY

(57) Abstract: The invention relates to methods for determining protein activity using NMR spectroscopy. The present invention provides a method for determining protein activity *in vivo* using probe compounds and enhancing the nuclear polarisation of NMR active nuclei present in the probe compounds (hereinafter termed "hyperpolarisation") prior to NMR analysis. The invention also provides mixtures of probe compounds for the above-mentioned method.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/NO 03/00125

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12Q1/00 G01R33/465 G01N24/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q G01R G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01 96895 A (COOK NEIL ;LOOKER MIKE (GB); BOSWORTH NIGEL (GB); KNOX PETER (GB);) 20 December 2001 (2001-12-20) abstract; claims 1-17 ----	1-23
Y	WO 00 40988 A (COOK NEIL ;KNOX PETER (GB); NYCOMED AMERSHAM PLC (GB); AXELSSON OK) 13 July 2000 (2000-07-13) abstract page 15, line 19 -page 16, line 10 ----	1-23 -/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

19 August 2003

Date of mailing of the international search report

- 5. 09. 2003

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/NO 03/00125

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>AKIRA K ET AL: "Direct nuclear magnetic resonance spectroscopic analysis of (13)C-labeled antipyrine metabolites in human urine."</p> <p>DRUG METABOLISM AND DISPOSITION: THE BIOLOGICAL FATE OF CHEMICALS. UNITED STATES JUN 2001, vol. 29, no. 6, June 2001 (2001-06), pages 903-907, XP002251641</p> <p>ISSN: 0090-9556 abstract page 903</p> <p>---</p>	1-23
A	<p>SCOTT R J ET AL: "Determination of a 'GW cocktail' of cytochrome P450 probe substrates and their metabolites in plasma and urine using automated solid phase extraction and fast gradient liquid chromatography tandem mass spectrometry."</p> <p>RAPID COMMUNICATIONS IN MASS SPECTROMETRY: RCM. ENGLAND 1999, vol. 13, no. 23, 1999, pages 2305-2319, XP002251642</p> <p>ISSN: 0951-4198 abstract page 2305, column 2, line 11 -page 2306, column 1, line 8</p> <p>---</p>	1-23
A	<p>STEVENS J C ET AL: "Use of the steroid derivative RPR 106541 in combination with site-directed mutagenesis for enhanced cytochrome P-450 3A4 structure/function analysis."</p> <p>THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS. UNITED STATES AUG 1999, vol. 290, no. 2, August 1999 (1999-08), pages 594-602, XP002251643</p> <p>ISSN: 0022-3565 abstract</p> <p>---</p> <p>-/-</p>	1-23

INTERNATIONAL SEARCH REPORT

Internal Ref.	Application No
	PCT/NO 03/00125

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KOUDRIAKOVA T ET AL: "In vivo disposition and metabolism by liver and enterocyte microsomes of the antitubercular drug rifabutin in rats." THE JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS. UNITED STATES DEC 1996, [Online] vol. 279, no. 3, December 1996 (1996-12), pages 1300-1309, XP002251644 ISSN: 0022-3565 Retrieved from the Internet: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uid.. [retrieved on 2003-08-15] abstract -----</p>	1-23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NO 03/00125

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: **1-10**
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 1-10

Claims 1-10 relate to a method of treatment of the human or animal body by surgery or by therapy/ a diagnostic method practised on the human or animal body/Rule. 39.1(iv). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compound/composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/NO 03/00125

Patent document cited in search report	Publication date		Patent family member(s)		Publication date
WO 0196895	A 20-12-2001	AU EP WO	6407201 A 1290461 A1 0196895 A1		24-12-2001 12-03-2003 20-12-2001
WO 0040988	A 13-07-2000	AU CA EP WO JP	1880300 A 2356442 A1 1141738 A1 0040988 A1 2002534687 T		24-07-2000 13-07-2000 10-10-2001 13-07-2000 15-10-2002